

REMARKS/ARGUMENTS

Claims 1-8 are pending. Claim 4 has been amended to include the chemical structure of formula III for clarification purpose, as the Examiner suggested. Support for this amendment can be found at, for example, page 4, lines 10-20. No new matter is entered.

Claim Rejections under 35 U.S.C. 103(a)

Claims 1-3 were rejected under 35 U.S.C. 103(a) as being unpatentable over Rossey (U.S. patent 4,794,185) in view of Sohda (U.S. patent 5,932,592).

Applicant respectfully traverses. In Rossey, the compound of formula I is made by reacting the compound of formula IV with thionyl chloride, followed by a step of reducing with a reducing agent such as NaBH₄, and ZnBH₄ (see col. 1 line 11- col. 2, line 3, and column 7, scheme). The secondary reference Sohda (U.S. patent 5,932,592) uses phosphorous tribromide to displace a primary alcohol to produce a primary bromide. In contrast, in the present invention (see claim 1), a compound of formula I or a salt thereof is made by reacting the intermediate compound III with phosphorus tribromide, followed by a step of hydrolysis (e.g. hydrolyzing by addition of water to the reaction media, see page 6, lines 9-11). As shown by its chemical structure, the intermediate of formula III of the present invention is obviously not a primary alcohol.

Firstly, as the Examiner acknowledged, the present invention differs from Rossey in that it uses phosphorous tribromide instead of thionyl chloride to react with the intermediate compound III. Neither the primary reference Rossey nor the secondary reference Sohda presents any problem of using thionyl chloride in its process. Hence, there is no motivation for a person of ordinary skill in the art to modify the process of Rossey by replacing thionyl chloride with phosphorous tribromide. Further, phosphorus tribromide is indeed a halogenating agent as the Examiner points out, but it usually only reacts with a primary alcohol to produce the primary

bromide, as used by Sohda. Hence, Sohda does not provide any motivation for a person of ordinary skill in the art to use phosphorous tribromide as a halogenating agent in producing the compound of formula III of the present application, which has a different chemical structure from the primary alcohol of Sohda.

Secondly and more importantly, Rossey requires the use of a reducing agent to reduce the intermediate formed by the reaction of thionyl chloride and the compound of formula I. Nowhere in Rossey does it teach a hydrolysis step for hydrolyzing the intermediate formed by the reaction of thionyl chloride and the compound of formula I. Hence, even if a person of ordinary skill in the art were to replace thionyl chloride with phosphorous tribromide, he or she still would have not arrived at the present invention comprising the hydrolysis step. As MPEP 2142 clearly states, to establish a proper *prima facie* obviousness rejection, the prior art (prior art references when combined), must teach or suggest all the claimed limitations. None of Rossey and Sohda teaches the limitation as to the hydrolysis step of the present invention. Therefore, the present invention is not obvious over Rossey in view of Sohda under 35 U.S.C. 103.

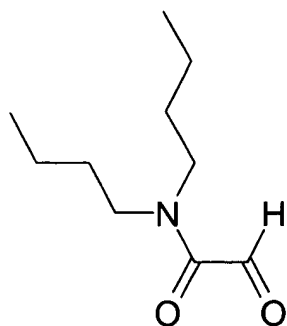
Moreover, the unexpected results of the present invention have been clearly presented in the specification, for example, at the paragraph bridging pages 5 and 6. It is surprising that upon the hydrolysis step, the desired 3-acetamide derivative is obtained directly and in good yield. The filtration and subsequent washing of the salt allows the removal of impurities and unreacted materials. Likewise, the hydrolysis of the filtered material is simplified due to the removal of the highly reactive phosphorous tribromide. Similarly the product can be isolated through direct hydrolysis of the reaction mixture.

Hence, claims 1-3 are not obvious over the cited prior art under 35 U.S.C. 103(a). Applicant respectfully requests that the Examiner withdraw this rejection.

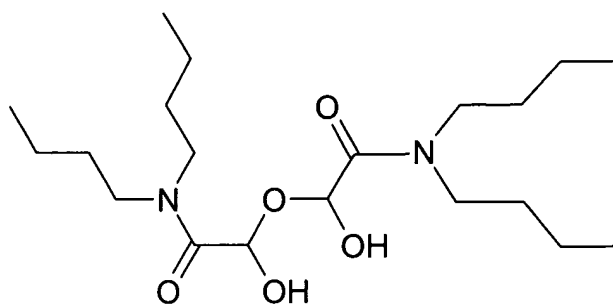
Claims 4-8 were rejected under 35 U.S.C. 103 (a) as being obvious over Rossey in view of George (U.S. Patent 4,808,594) and Whitfield (GB 793807) and Perez (J. Org. Chem. 1988 53: 408-4132). Applicant respectfully disagrees.

Firstly, none of these cited references suggests any problem of using the acetamide compound of formula (III) of Rossey. Nor does any of these references disclose any advantage of using dialkylglyoxylamide over the compound of formula (III) of Rossey. Hence, none of these cited references provides any motivation for a person of ordinary skill in the art to modify the process of Rossey by substituting the compound of formula (III) with dialkylglyoxylamide to arrive at the present invention. Further, George reacts dialkylglyoxylamide with a compound of formula (V) that is structurally different from the compound of formula (III) of Rossey. This fact further supports that there is no motivation for a person of ordinary skill in the art to make any modification of the process of Rossey based on the teachings of George.

Secondly and more importantly, dialkylglyoxylamide of George is not the compound of formula (II) of the present invention. Taking the dibutylglyoxylamide as an example, it may be two different compounds assigned with different CAS registry numbers, and having different chemical structures as shown below.



A (Registry Number 11689-11-3)



B (Registry Number 146829-87-0)

As above shown, the compound of formula A is a monomer; whereas the compound of formula B is a dimer. These two kinds of compounds have totally different physical and chemical properties. The dimer compound of formula B is very stable. For example, the hemi-acetal dimer of N,N-dialkylglyoxylamide of formula (II) of the present invention has a melting point of approximately 120⁰C. It is not clear in the prior art that such a substance would undergo the required condensation reaction of the present invention. By contrast, the monomer formula A is a very active compound with a free aldehyde group. Such a monomer of formula A is usually formed in a solution after strong acid hydrolysis of the corresponding stable dimethyl or diethyl acetal compound.

As the Examiner stated, George merely mentions "N,N-dialkyl(R₁,R₂)-glyoxylamide, but does not provide its chemical structure (col. 2, line 60). However, in example 1 of George, N,N-dimethylglyoxylamide diethyl acetal is reacted with concentrated hydrochloric acid in the media of acetic acid for 2 hours at 50⁰C. This clearly shows that the dialkylglyoxylamide of George is an active monomer with an aldehyde group.

By contrast, the present invention does not require acid hydrolysis as it is done under essentially anhydrous, neutral or slightly basic conditions (provided by the imidazo[1,2-a]pyridine substrate itself) (see example 1).

Since George does not teach a compound of formula II of the present invention, even if a person of ordinary skill in the art were to modify the process of Rossey as the Examiner proposed, he or she would still not have arrived at the present invention. Hence, the present invention is not obvious over Rossey in view of George and other references cited by the Examiner.

Moreover, as the specification discusses (see e.g. page 5, lines 10-20), the present invention has unexpected results compared to the prior art. For example, one interesting advantage of the present invention is that the product formed in this step (the acetamide) can be carried directly into the next step (reacting with phosphorous tribromide) of the process without isolation. In addition, as above discussed, using an active compound of George with a free aldehyde group falls within common knowledge of a person of ordinary skill in the art, and the results are expected; while using a stable compound of formula II of the present invention is not expected by a person of ordinary skill in the art. In fact, many attempts to repeat the claimed yield of the prior art produced incomplete reactions requiring the chromatographic removal of the starting substrate. On the other hand, the present invention allows for complete conversion of the substrate and extremely easy reaction workup. The present invention is a great improvement over the prior art.

Hence, claims 4-8 are not obvious in view of the prior art under 35 U.S.C. 103 (a).
Withdrawal of such a rejection is respectfully requested.

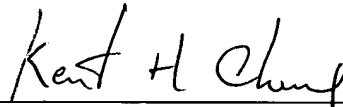
Claim rejections under 35 U.S.C. 112 second paragraph

Claims 4-8 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the structure of formula III was not presented in independent claim 4, although it has been presented in claim 1. In response, the structure of formula III has been added in the present claim 4. Hence, the indefiniteness rejection of claim 4 should be overcome by the present amendment.

Based on the foregoing, Applicant believes that the present application is in condition of allowance. Early and favorable action is earnestly requested.

It is believed that no fees or charges are required at this time in connection with the present application; however, if any fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,
COHEN, PONTANI, LIEBERMAN & PAVANE

By 
Kent H. Cheng, Reg. No. 38,849
551 Fifth Avenue, Suite 1210
New York, New York 10176
(212) 687-2770

Dated: July 8, 2004